USA FDA CLINICAL TRIAL DATA BIB

ASMBS Obesity Weekend
June 25-27, 2015
Las Vegas, Nevada
Helmuth T. Billy, MD
Ventura Advanced Surgical Associates.

BIB (BIOENTERICS INTRAGASTRIC BALLOON AKA ORBERA™)

PIVOTAL STUDY DESIGN (IBm005)

- Multi-center, prospective, randomized, non-blinded, controlled trial
- 1:1 randomization (ORBERA™ + Behavioral Modification versus Behavioral Modification alone)
- 15 sites
- 448 subjects enrolled; 273 patients randomized
- 12 month follow-up

Primary Objective
- Evaluate the safety and effectiveness of the device as an adjunct to behavioral modification for patients with a BMI ≥30 and ≤40

Secondary Objectives
- Assess changes in obesity-related comorbidities and QOL
- Assess change in weight and BMI, depressive symptoms, eating behavior, comorbidities, and the impact on gastric emptying

OVERVIEW OF INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria
- BMI ≥30 and ≤40
- Male or female
- Ages 18 – 65
- History of obesity for at least two years and have failed more conservative weight-reduction alternatives, such as diet, exercise, and behavioral modification programs
- History of GI surgery, IBS, Crohn's, gastritis, GI bleeding, bowel obstruction, etc.
- History of dysmotility or delayed GE
- MI, anemia, unstable thyroid disease
- Untreated psychiatric or eating disorders (e.g., bulimia)
- Type 1 diabetes
- Positive H. pylori at screening
- Hiatal hernia ≥ 2cm

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SUBJECT DISPOSITION

Enrolled 445
- SF After Randomization 12
- D/C Before Week 52 27
- Completed Study - w52 93

Screen Failures 131
- Treatment 137
- Control 136
- Drop-Outs After Randomization 6

SUBJECT DEMOGRAPHICS

- 90% female
- Mean age at study entry = 38.7 years
- 81% Caucasian
- 70% married
- Mean excess weight at baseline = 78.80 lbs
- Mean BMI at baseline = 35.2

DISCLOSURES 2014, 2015

- Transenterix – Consultant
- Johnson and Johnson – Speaker
PROTOCOL-DEFINED CO-PRIMARY EFFECTIVENESS ENDPOINTS

- **Co-Primary Endpoint #1 – EWL**
  - Mean %EWL (95% CI) ≥25% at 9 months
  
  RESULT = *35.98% EWL (29.72%, 42.24%)
  \( p < 0.001 \)

- **Co-Primary Endpoint #2 – Superior to Diet & Exercise (Control)**
  - ≥30% of BIB® subjects will experience ≥15% EWL over the mean %EWL of the control group at 9 months
  
  RESULT = *48.4% (37.74%, 59.07%)
  Note: mean %EWL of the control group was 9.67%
  \( p < 0.001 \)

*Using BMI 25 as IBW

RESULT = *35.98% EWL (29.72%, 42.24%)
\( p < 0.001 \)

RESULT = *48.4% (37.74%, 59.07%)
\( p < 0.001 \)

GREATER WEIGHT LOSS IN ORBERA™ GROUP THROUGH 12 MONTHS

<table>
<thead>
<tr>
<th>Month</th>
<th>ORBERA™</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10.2%</td>
<td>9.1%</td>
</tr>
<tr>
<td>3</td>
<td>4.1%</td>
<td>3.6%</td>
</tr>
<tr>
<td>6</td>
<td>4.0%</td>
<td>4.0%</td>
</tr>
<tr>
<td>9</td>
<td>3.6%</td>
<td>7.4%</td>
</tr>
<tr>
<td>12</td>
<td>3.6%</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

% of Patients (95% CI)

- ≥5% WL
- ≥7% WL
- ≥10% WL

SAFETY IN THE ORBERA™ PIVOTAL TRIAL

- Mild: easily tolerated
- Moderate: caused discomfort
- Severe: unable to do normal activities

- There were no deaths or unanticipated adverse device effects (UADEs).
- Placement of the device within the stomach produces an expected and predictable reaction of nausea, vomiting, gastroesophageal reflux, pain, and cramping.
- The most common AEs were nausea, vomiting, abdominal pain, and GERD.
  - Generally mild to moderate in severity, typically resolving within 7 days
- The most common device-related SAE was device intolerance (8 events)—all resolved without sequelae (residual symptoms or pathology).
- One subject had a procedure-related SAE that resolved without sequelae (laryngospasm during device removal).

MOST FREQUENT ADVERSE EVENTS ARE NAUSEA, VOMITING & GASTRIC PAIN

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>83%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>74%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>61%</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>26%</td>
</tr>
<tr>
<td>Belching</td>
<td>23%</td>
</tr>
<tr>
<td>Constipation</td>
<td>22%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22%</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>17%</td>
</tr>
<tr>
<td>Abdominal pain upper</td>
<td>17%</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>14%</td>
</tr>
<tr>
<td>Constipation</td>
<td>14%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>11%</td>
</tr>
</tbody>
</table>

Source: US Pivotal Trial

DEVICE REMOVALS PRIOR TO SIX MONTHS

- 19 patients (15.1%) had ORBERA™ removed prior to Month 6 due to adverse events.
- Study protocol did not allow physicians to use medications to treat any symptom.

Lessons learned in peri-procedural management and diet advancement should demonstrate a lower rate of early device removal in a post-approval setting. OUS experience is 5% to 7%.
US PIVOTAL STUDY CONCLUSIONS

• ORBERA™ led to significantly greater weight loss than behavior modification alone.
• ORBERA™ has been shown to produce weight loss that is preserved even after device removal.
  - More than 70% of weight loss at 6 months was maintained through 12 months, on average.
• Weight loss led to significant improvements in quality of life.
• ORBERA™ helped patients improve control over their eating behaviors.

This trial demonstrates that ORBERA™, in combination with a weight management program, is an effective weight loss tool for individuals with obesity.